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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,384	08/20/2002	Maria Laura Gennaro	07763-042001	7084
26211 7590 01/29/2007 FISH & RICHARDSON P.C. P.O. BOX 1022 MINNEAPOLIS, MN 55440-1022			EXAMINER SWARTZ, RODNEY P	
			ART UNIT	PAPER NUMBER
			1645	
			MAIL DATE	DELIVERY MODE
			01/29/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b> <b>Before the Filing of an Appeal Brief</b>	<b>Application No.</b> 10/009,384	<b>Applicant(s)</b> GENNARO ET AL.	
	<b>Examiner</b> Rodney P. Swartz, Ph.D.	<b>Art Unit</b> 1645	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 28June2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
 b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on 28June2006. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

#### AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
 (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
 (b) ☐ They raise the issue of new matter (see NOTE below);  
 (c) ☒ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
 (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
 5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
 6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
 7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
 The status of the claim(s) is (or will be) as follows:  
 Claim(s) allowed: none.  
 Claim(s) objected to: \_\_\_\_\_.  
 Claim(s) rejected: 1-8, 11-20.  
 Claim(s) withdrawn from consideration: \_\_\_\_\_.

#### AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
 9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing of good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
 10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

#### REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: \_\_\_\_\_.  
 12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
 13. ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. Applicants' Notice of Appeal, received 28 June 2006, is acknowledged. Applicants' Response to Final Office Action, received 28 June 2006, is acknowledged. Applicants proposed amendment of claims 17-20 and cancelation of claims 21-36 will not be entered because the amendments of claims 17, 19, and 20 are improper.

Claim 17 inserts "segment" in step b immediately following "polypeptide" without underlining.

Claim 19 inserts "polypeptide segment" in step b without underlining, and deletes "composition" without brackets or strikethrough.

Claim 20 inserts "polypeptide segment" in step b without underlining, and deletes "composition" without brackets or strikethrough.

2. However, in order to expedite prosecution, the examiner has considered the response as if the claims were properly amended.

#### **Rejections Maintained If Amendments were Properly Entered**

3. The rejection of claims 17-20 under 35 U.S.C. 112, first paragraph, scope of enablement for diagnostic methods utilizing polypeptides, is maintained for reasons of record.

Applicants argue that the specification is sufficient support for the scope of the claims, and that one of ordinary skill in the art would have expected a substantial number of the secreted *M. tuberculosis* polypeptides of the claimed methods to be useful in the diagnosis of tuberculosis. Applicants submitted a review article by A.S. Mustafa as support for their argument, and continue to rely on the prior submission of a reference by Amor et al.

The examiner has considered applicants' arguments and the two cited references, but does not find them persuasive.

The reference by Amor et al is directed to ELISA *in vitro* assays to determine if sera from TB patients contain antibodies which bind to the polypeptides utilized. The reference and applicants' arguments concerning this reference are drawn to criticalities not found in the instant claims. The instant claims are drawn to an *in vivo* assay in which the polypeptides are administered to a subject and examining said subject for an immune response to said polypeptides, i.e., a skin test which is directed toward cell mediated immune response, not antibody mediated immune response. In addition, Amor et al did not test sera from: 1) patients with BCG vaccination, 2) patients with non-*M. tb* mycobacterial infections, nor 3) patients with past *M. tb* infections.

The reference by Mustafa is a review article which merely indicates that some polypeptides of *M. tuberculosis* origin may show promise as new diagnostic agents, i.e., an invitation to experiment without a reasonable expectation of success.

4. The rejection of claims 1-8 and 11-20 under 35 U.S.C. 112, second paragraph, indefiniteness for specific properties is maintained for reasons of record.

Applicants argue that the Amor et al reference teaches that the claimed polypeptides are specifically expressed by bacteria of the *M. tuberculosis* Complex and therefore, it is likely that antibodies elicited by these polypeptides would not detect infections by mycobacteria other than those of the *M. tuberculosis* Complex.

The examiner has considered applicants' argument in light of the reference by Amor et al, but does not find it persuasive. Firstly, Amor et al did not test sera from: 1) patients with BCG vaccination, 2) patients with non-*M. tb* mycobacterial infections, nor 3) patients with past *M. tb* infections. Thus, the specificity of the antibodies detected is not determined to be *M. tb* specific. Secondly, applicants' argument is directed to a criticality not being claimed, i.e.,

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applicants now include other species in their argument that the polypeptides would not detect infections by mycobacteria other than those of the *M. tuberculosis* Complex. The claims recite that the polypeptides have specific antigenic and immunogenic properties only to *M. tuberculosis*. The *M. tuberculosis* complex comprises other species of *Mycobacteria* in addition to *M. tuberculosis*.

Applicants' argument that the specification provides support for the *M. tuberculosis* specificity (page 7, lines 18-22; page 7, line 30 to page 8, line 3) constitutes merely a proposed attribute of a polypeptide. However, there is no evidence in the specification that the claimed DNA molecules actually encode polypeptides with any of the hoped for specificity.

### **Conclusion**

5. Claims 1-8 and 11-20 remain rejected.
6. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rodney P. Swartz, Ph.D., Art Unit 1645, whose telephone number is (571) 272-0865. The examiner can normally be reached on Monday through Thursday from 9:00 AM to 7:30 PM EST.

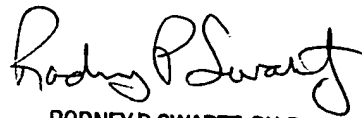
If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Jeffrey Siew, can be reached on (571)272-0787.

The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



RODNEY P SWARTZ, PH.D  
PRIMARY EXAMINER

Art Unit 1645

January 24, 2007